2) SCIENTIFIC ABSTRACT OF THE CLINICAL PROTOCOL

The plasmid pVGI.1(VEGF2) contains the deoxyribonucleic acid sequence for vascular endothelial growth factor 2 (VEGF-2), a member of a class of natural growth factors that promote angiogenesis. The Sponsor has studied VEGF-2 gene transfer, delivered either via an epicardial approach via a mini-thoracotomy during surgery or via an endocardial approach using a percutaneous transvalvular cardiac catheter. These studies were conducted in patients with refractory, stable Canadian Cardiovascular Society class III or IV angina who were not considered to be suitable candidates for conventional revascularization procedures. These preliminary studies have indicated that intramyocardial delivery of pVGI.1(VEGF2) at doses up to and including 2 mg are safe and may be associated with improvements in exercise tolerance and in angina class. The present study will evaluate a single dose of pVGI.1(VEGF2) (800 µg) in an open-label fashion in up to seven patients who were previously randomized to placebo treatment in study VEGF2-CAD-CL-005.

This study will enroll patients who are considered to have refractory, stable Canadian Cardiovascular Society class III or IV angina who are not suitable candidates for conventional revascularization procedures.

The primary efficacy objective of this study is to assess the effect of a 800 µg intra-myocardial dose of pVGI.1(VEGF2) when given by using an injection cardiac catheter on the change from baseline in exercise duration at 3 months after treatment.

The secondary objectives of this study are to assess the effect of the dose of pVGI.1(VEGF2) on the change from baseline in angina class, NTG use, myocardial perfusion by SPECT, and patient functional status Seattle Angina Questionnaire (SAQ) at 3 months after treatment. In addition the changes in exercise duration, angina class, and patient functional status will be evaluated at intervals over the 1-year Follow-up Period.

The safety of pVGI.1(VEGF2) will be evaluated on an ongoing basis over the duration of this study by the sponsor.

The study will consist of an optional Run-in Period, a Baseline Period (up to 4 weeks), a Treatment Period (Days 1 through 3), a Post-treatment Period (Out to Month 12) during which the study objectives will be evaluated for protocol defined outcomes. The protocol will be followed by a Long-term (up to 15 year) Post-Treatment Follow-up phase. The Run-in Period may be waived if documentation indicates that a potential patient is currently taking maximally tolerated doses of multiple anti-anginal medications selected from one or more of the following three classes of drugs: nitrates, 13-blockers, and calcium channel antagonists. Up to 7 patients may be enrolled at 2 treatment sites. After determination of an individual subject's final eligibility the patient may be enrolled into the study. Patients will receive a single 800 tg dose of pVG1.1(VEGF2). Study drug will be administered to patients by injection into the myocardium by using an experimental cardiac catheter advanced percutaneously, transvalvular into the left ventricle. After dosing patients will remain in hospital for 24 hours observation and may remain in hospital for up to three days. Following discharge from hospital the patients will return at weeks 1, 2 & 4 and months 2, 3, 6, 9, and 12 of the post-treatment period for follow-up efficacy and safety assessments. All patients will remain on their pre-study regimen of anti-anginal medications unless modifications are medically necessary. Following the formal Post-treatment evaluation period patients will have annual follow-up evaluations (up to 15 years). The longterm follow-up evaluations phase will consist of annual evaluations to be completed by either the Investigator or the patient's personal physician.

Safety will be assessed by evaluation and comparison of baseline and follow-up parameters, to include, physical examination, 12-lead electrocardiogram, transthoracic echocardiogram, vital signs (temperature, blood pressure, heart rate and respiration), hematology, clinical chemistry, urinalysis, concomitant medications, plasma VEGF-2 concentrations, serum antibody to VEGF-2, and the monitoring of adverse events. The long-term (up to 15 year) follow-up of patients will assess changes from baseline observed in the patient's health as detected during routine annual follow-up visits to the physician. During these visit the investigator will request from the patient information regarding various routine tests the patient may have had during the course of the previous year. These long term follow-up data points may include the results of any tests the patient may have had during the preceding year, i.e. X-rays, ophthalmologic evaluations, PAP smears, PSA test results, laboratory tests. In addition to these tests the investigator should also complete a physical examination of the patient and obtain information regarding any medical events that may be classified as Serious Adverse Events by FDA or NTH definition as found in the regulations.

The data will be tabulated, analyzed and presented in an individual case study format. As patients were previously enrolled as placebo treatment patients in a similar protocol they may serve as their own controls.